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T. TUCK
PATENT #30
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Attorney Dock t No. 02481.1403-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

Ulrich STACHE et al.

Serial No.: 08/897,455

Filed: July 22, 1997

For: CORTICOID-17, 21-DICARBOXYLIC ESTERS
AND CORTICOSTEROID 17-CARBOXYLIC
ESTER 21-CARBONIC ESTERS, PROCESSES
FOR THEIR PREPARATION AND
PHARMACEUTICALS CONTAINING THESE
COMPOUNDS



TECH CENTER 1600/2900

Group Art Unit: 1616

Examiner: B. Badio

BOX AF

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

REPLY BRIEF UNDER 37 C.F.R. § 1.193

Appellants present the following arguments in reply to the Examiner's Answer dated November 18, 1999.

I. The Prior Art Did Not Guide Those Skilled In The Art To The Claimed Invention

Claims 1, 4-5, and 7-10 are rejected as obvious under 35 U.S.C. § 103(a) over U.S. Patent No. 4,655,971 to Page et al. ("Page"). The Examiner maintained that the claimed compounds were obvious, stating that the compounds may be derived by selecting particular values for the substituents in the general formula of Page. For example, with respect to the portion of the Page compounds that correspond to the 21-position substituent of the claimed compounds, the Examiner stated that R_5 of Page may be $OC(O)-R'$, wherein R' is an alkyl group of 1 to 16 carbon atoms, a phenyl group, or an aralkyl group of 7 to 8 carbon atoms. The Examiner concluded that applicant's 21-position substituent was within the scope of the Page disclosure and was obvious.

As explained in detail in appellants' Appeal Brief, one reason why the present claims were not obvious is because, contrary to the Examiner's position, the prior art did not suggest at least the particular substituent on the 21-position of the claimed

compounds. The Examiner's position outlined above does not tell the whole story, but merely follows a path cut through the forest by the appellants, not by the prior art. In fact, conspicuously missing in the Examiner's outline is any reference to the full scope of substituent combinations that are disclosed in Page, and any explanation as to why the prior art guided one skilled in the art through path created by the appellants.

Following the various definitions of the substituents at col. 1, lines 32-55 of Page, one skilled in the art must have defined R_5 as R_6 , instead of as a hydroxyl group. Then, R_6 must have been defined as OR_7 , instead of as a hydrogen or as one or two halogen atom substituents, where R_7 is an acyl group of the formula $R'CO$. Next, R' must have been defined as an aralkyl group of 7 to 8 carbon atoms, instead of a straight, branched, or cyclic alkyl group of 1 to 16 carbon atoms and instead of a phenyl group. Just the choice of R' alone involves a selection from a huge number of possibilities, including all possible permutations of 1 to 16 carbon atom straight, branched, or cyclic alkyl groups! The selection of variables is made even more difficult with respect to claims 9 and 10, which are narrower than claim 1, embrace the compounds of Examples 23 and 59 in the specification, and require selection of a number of variables outside the 21-position.

Even if the Examiner has made a showing of a *prima facie* case of obviousness, the claimed compounds possess properties that distinguish the claims as a whole from the prior art. The specification states that compounds having a 21-aryl ester or 21-hetaryl ester, in particular, "often exhibit qualities of effect which are clearly superior, as regards the local/systemic ratio of antiinflammatory effect, to those of structurally related corticoid 17,21-dicarboxylic esters or structurally related corticoid 17-alkyl carbonate 21-carboxylic esters which do not carry any aryl or hetaryl group in the 21-acid residue." Specification at page 5, lines 20-29. The specification at page 13, lines 20-30 also states that the compounds "surprisingly" exhibit "a very good ratio of local to systemic antiinflammatory effect, which ratio is often markedly superior . . . to that of known corticoid 17-alkyl carbonate 21-esters, which do not carry any aryl or hetaryl group in the 21-ester radical, such as, for

example, 21-ester groups having a 21-alkyl group." Detailed pharmacological testing in support of these statements appears in the specification at page 15, line 12 to page 19, line 16. As this information was in the application as filed, this is evidence of record and must be considered in this case.

The "markedly superior" ratio of local to systemic antiinflammatory effect of the claimed compounds constitutes part of the invention "as a whole," and rebuts any *prima facie* case that the Examiner alleges to have established. As noted by the Federal Circuit, the properties of claimed compounds compared to prior art compounds must be given weight in analyzing the obviousness of the invention as a whole: "[c]learly, in determining patentability the Board was obligated to consider all the evidence of the properties of the claimed invention as a whole, compared with those of the prior art." In re Dillon, 16 U.S.P.Q.2d 1897, 1902 (Fed. Cir. 1990), decided *in banc*. Moreover, the Examiner is reminded that the obviousness determination must be considered all over again in light of these unexpected properties, as opposed to simply determining whether the asserted properties outweigh any pre-conceived conclusion of obviousness. See MPEP § 2144.08 ("A determination under 35 U.S.C. 103 should rest on all the evidence and should not be influenced by any earlier conclusion. . . . Thus, once the applicant has presented rebuttal evidence, Office personnel should reconsider any initial obviousness determination in view of the entire record.").

Considering the "markedly superior" properties of the claimed compounds compared to the prior art, together with the lack of guidance in the prior art to derive the compounds from a purely structural standpoint, the invention "as a whole" was not obvious to those skilled in the art, and the rejection should be reversed.

II. The Comments In The Examiner's Answer Do Not Fill The Gaps In The Attempted Showing Of Obviousness

The Examiner's Answer stated that appellants' arguments in the Appeal Brief in favor of the patentability of the claims were not persuasive for a number of reasons.

First, the Examiner stated that appellants' arguments "center around the working examples of Page," but that the reference should instead be "evaluated based on what it teaches one having ordinary skill in the art and not on the exemplified compounds shown in the prior art."

In response to this first point, appellants disagree that their arguments center around the working examples of Page. Appellants argued that the prior art would not have guided one skilled in the art to derive the claimed compounds. This argument hits squarely with the standard for determining obviousness, namely, whether "the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a). Relevant to this inquiry is what the Page disclosure taught one skilled in the art, including whether the specific examples guided those skilled in the art through the generic disclosure to obtain the present compounds. As evidence that Page did not guide those skilled in the art in that direction, appellants noted that none of the examples in Page teaches the particular -O-CO-[(C₁-C₄)-alkyl]-phenyl substituent in the 21-position of the claimed compounds, let alone the combination of that substituent with other substituents needed to be chosen to match the remaining positions of the compounds. The decisions of In re Baird and In re Jones support appellants' arguments relating to the specific examples of Page.

Second, the Examiner maintained that the claimed compounds differ from Examples 9 and 19 of Page only with respect to the -O-CO-[(C₁-C₄)-alkyl]-phenyl substituent in the 21-position. The Examiner concluded that one skilled in the art would only need to make one substituent swap, rather than make a selection of all substituents in the claimed compounds, and that this one swap would be obvious to one skilled in the art. As outlined in the first section, however, Page teaches a huge number of possibilities for what corresponds to the 21-position of the claimed compounds. Rather than merely being one substitution swap from Examples 9 and 19, Page discloses what applicants believe to be over a thousand possibilities in the 21-position alone.

Third, the Examiner argued that the decisions of In re Baird and In re Jones are not applicable to appellants' claims, contending that the pending claims encompass numerous compounds in Markush format, and the claims on appeal in Baird and Jones were directed only to a specific compound. Section 2144.08 of the MPEP, however, relies on In re Baird in formulating the examination procedures for determining the obviousness of either a single species or a subgenus of a prior art disclosure. The Examiner's interpretation of In re Baird as applicable only to claims directed to a single species compound is therefore at odds with the interpretation of In re Baird given by the Patent and Trademark Office. Appellants should therefore be entitled to rely on the reasoning of In re Baird and In re Jones for all the pending claims.

Fourth, the Examiner stated that the appellants "intended the inclusion of compounds having other than an aralkyl ester group in the 21-position," citing Examples 3-5 on pages 21-22 of the specification. What matters now for the obviousness inquiry is what is claimed now. Appellants have a right to claim less than everything disclosed in the specification, and it is irrelevant whether subject disclosed but not claimed would have been obvious or not.

Fifth, the Examiner stated that a number of other issued patents cited by the appellants were not relevant to the patentability of the claims, since those patents did not suggest the equivalence of an aralkyl ester group or other acyl group attached to the 21-position as taught by Page. Since the obviousness determination is made with reference to what the prior art as a whole taught those skilled in the art, those documents are relevant to the present case. As noted by the Examiner, none of the patents teaches the 21- position substitution used by the appellants in the present claims, and the patents are properly used as evidence that the art did not guide one skilled in the art to the claimed compounds.

CONCLUSION

For the reasons set forth above, appellants maintain that the Examiner has not established a *prima facie* case of obviousness based on Page. Appellants also note that any *prima facie* case of obviousness, if it were to exist, is rebutted by the showing of superior properties of the compounds of the invention. Accordingly, appellants respectfully request reversal of the rejection of claims 1, 4-5, and 7-10 under 35 U.S.C. § 103(a).

If there is any fee due in connection with the filing of this Reply Brief, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.



By: _____

Steven J. Scott
Reg. No. 43,911

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